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Late Causes of Death After Pediatric Cardiac Surgery

A 60-Year Population-Based Study

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ABSTRACT

BACKGROUND Comprehensive information regarding causes of late post-operative death following pediatric congenital cardiac surgery is lacking.

OBJECTIVES The study sought to analyze late causes of death after congenital cardiac surgery by era and defect severity.

METHODS We obtained data from a nationwide pediatric cardiac surgery database and Finnish population registry regarding patients who underwent cardiac surgery at <15 years of age at 1 of 5 universities or 1 district hospital in Finland from 1953 to 2009. Noncyanotic and cyanotic defects were classified as simple and severe, respectively. Causes of death were determined using International Classification of Diseases diagnostic codes. Deaths among the study population were compared to a matched control population.

RESULTS Overall, 10,964 patients underwent 14,079 operations, with 98% follow-up. Early mortality (<30 days) was 5.6% (n = 613). Late mortality was 10.4% (n = 1,129). Congenital heart defect (CHD)–related death rates correlated with defect severity. Heart failure was the most common mode of CHD-related death, but decreased after surgeries performed between 1990 and 2009. Sudden death after surgery for atrial septal defect, ventricular septal defect, tetralogy of Fallot, and transposition of the great arteries decreased to zero following operations from 1990 to 2009. Deaths from neoplasms, respiratory, neurological, and infectious disease were significantly more common among study patients than controls. Pneumonia caused the majority of non-CHD-related deaths among the study population.

CONCLUSIONS CHD-related deaths have decreased markedly but remain a challenge after surgery for severe cardiac defects. Premature deaths are generally more common among patients than the control population, warranting long-term follow-up after congenital cardiac surgery. (J Am Coll Cardiol 2016;68:487–98) © 2016 by the American College of Cardiology Foundation.

The first pediatric cardiac surgery in Finland was performed in 1953. Since then, >13,000 patients have undergone >16,000 operations in Finland. Data on all operations and patients are stored in a nation-wide pediatric cardiac surgical database. We previously found that the life expectancy of patients after congenital cardiac surgery remained lower than the general population, despite significant improvements in both early and late results (1). This was particularly true among patients with severe cardiac defects such as tetralogy of Fallot (TOF), transposition of the great arteries (TGA), hypoplastic left heart syndrome (HLHS), and univentricular heart (UVH) (1).

Patients with congenital cardiac defects often require extensive long-term follow-up, and information about the causes of death among these patients may improve their clinical management during

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ABBREVIATIONS AND ACRONYMS

ASD = atrial septal defect
ASO = arterial switch operation
CHD = congenital heart defect
CI = confidence interval
COA = coarctation of the aorta
HLHS = hypoplastic left heart syndrome
HR = hazard ratio
PDA = patent ductus arteriosus
RR = rate ratio
TGA = transposition of the great arteries
TOF = tetralogy of Fallot
UVH = univentricular heart
VSD = ventricular septal defect

follow-up. However, a limited number of studies exist on this subject. In this study, we investigated the nationwide causes of patient deaths up to 60 years after their first cardiac operation, and compared them to deaths in the general population to identify areas that require special attention during the long term.

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METHODS

The Finnish Ministry of Social Affairs and Health granted permission for this study, and the ethical committee approved the research protocol.

PATIENTS AND DATA COLLECTION. We used the custom-built ProCardio version 8 database, the Research Registry of Pediatric Cardiac Surgery (Melba Group, Helsinki, Finland) running on Filemaker Pro version 8.5 (Filemaker Inc., Santa Clara, California), to obtain patient and operational data. The database contains the records for all pediatric patients undergoing surgery for congenital heart defects (CHDs) at 5 university hospitals (Helsinki, Kuopio, Oulu, Tampere, and Turku) and 1 district hospital (Aurora Hospital, Helsinki) in Finland. The Finnish Population Registry provided the status and date of death for all patients.

We included all pediatric cardiac operations performed between 1953 and 2009 in Finland on children who were under 15 years of age at the time of their first operation. Follow-up began after the first cardiac surgery of the patient, and ended at death, emigration, or on December 31, 2012. The only procedures excluded were patent ductus arteriosus (PDA) closures in children <1 month of age, and pacemaker implantations in patients for whom this was the only procedure.

Each patient was assigned 1 primary diagnosis from a severity-based hierarchical list of cardiac defects: PDA, atrial septal defect (ASD), coarctation of the aorta (COA), ventricular septal defect (VSD), TOF, TGA, HLHS, and UVH. All remaining cardiac defects were collectively referred to as miscellaneous. For patients with several cardiac defects, we chose the hierarchically more severe condition. For the sake of comparison, we dichotomized defect severity into simple (PDA, ASD, COA, and VSD) and severe (TOF, TGA, HLHS, and UVH) defects according to the lack or presence of cyanosis, respectively.

MORTALITY AND CAUSES OF DEATH. We excluded all early deaths (within 30 days post-operatively) from analyses regarding causes of death and incidence of death. For patients that emigrated, we marked the day of emigration as the last day of follow-up in survival analyses. Unclear causes of death were confirmed by autopsy. We obtained diagnosis codes for all deceased patients from Statistics Finland. Causes of death were categorized into CHD-related and non-CHD-related deaths. CHD-related deaths were classified as diseases within the Q20 to Q28 range from the International Classification of Diseases-10th Revision diagnosis system (and International Classification of Diseases-9th Revision numbers 745 to 747 for older cases).

We further categorized all CHD-related deaths into heart failures, sudden deaths, post-reoperative early deaths (<30 days), and cardiovascular deaths according to a previous classification system (2). Sudden deaths included all unwitnessed deaths that occurred during sleep and cardiovascular-related deaths occurring within 1 h of onset (or the significant worsening) of symptoms. Post-reoperative early death spanned all early operative deaths (within 30 days) after the patients' subsequent reinterventions. We classified the remaining causes of death not covered by other classes as cardiovascular.

We compared survival and the incidence of different CHD-related deaths by decade of operation to assess advances in late surgical outcome. Due to the small number of patients undergoing surgery for HLHS before the 1990s, we excluded such cases from the comparison of time periods.

Statistics Finland supplied us with 4 age-, sex-, time of birth-, and hospital district-matched control subjects from the general population for each study patient. We then compared the modes of non-CHD-related deaths of study patients to those among the general population, presenting results as rate ratios (RRs).

STATISTICS. We analyzed mortality by Poisson regression models utilizing a Lexis-type data structure with 3 time scales, vis-à-vis age, calendar year, and time since surgery (3). We report RRs on the basis of the Poisson regression with 95% confidence intervals (CIs). In the estimation of hazard rate curves, we used splines to produce smoothed curves with a 95% confidence envelope. Standard deviations are reported with mean values. Survival data is presented in the form of Kaplan-Meier plots, and 2-tailed p values obtained with the log-rank test; p values <0.05 were considered significant. All data analyses were carried out using the R program (R Development Core Team, Vienna, Austria, 2011) and IBM SPSS Statistics version 23.0 (SPSS, Inc., Chicago, Illinois).